## REMARKS

Claims 5 and 8 have been amended. Claims 12-14 have been cancelled without prejudice. No new matter has been added. Claims 1 to 12 are pending. Claims 1 and 8 are independent.

**Rejection under 35 U.S.C. § 112, second paragraph**

Claims 5 and 8 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. See page 2 of the Office Action. Applicants have amended claims 5 and 8 to address the issue raised by the Examiner. Applicants respectfully request reconsideration and withdrawal of this rejection.

**Rejection under 35 U.S.C. § 102(b) or 35 U.S.C. § 103(a)**

Claims 1-11 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Japan Patent No. 7-318,551 ("JP '551"). The Examiner states that

> [t]he claims are considered to read on Japan Patent No. 7-318,551. However, if a difference exists between the skims and Japan Patent No. 7-318,551, it would reside in optimizing the steps of Japan Patent No. 7-318,551. It would have been obvious to optimize the steps of Japan Patent No. 7-318,551 to enhance separation. (See page 2 of the Office Action.)

**Independent claim 1 and claims that depend therefrom**

Applicants have discovered a method for separating substances. The method includes separating substances using a stationary phase including **a charged polymer or copolymer and makes it possible to change the effective charge density on the surface of the stationary phase by a physical stimulus**. See independent claim 1. The physical stimulus changes the charged state of the effective charge density on the surface of the carrier, making it possible to perform two chromatographic modes, for example, ion-exchange chromatography and reversed phase chromatography, with the stationary phase. See page 6, lines 1-9 of the specification. Substances which have not been able to be separated by conventional methods can be separated by the method of claim 1. See, for example, page 4, lines 16-23 and page 6, lines 17 through page 7, line 6 of the specification.

JP '551 discloses a chromatographic material to the surface of which a bulking agent is bonded. See paragraph 8 of JP '551. JP '551 does not describe a charged stationary phase. The

chromatographic material of JP '551 does not possess a charged polymer or copolymer that changes the effective charge density on the surface of the stationary phase by a physical stimulus. JP '551 does not describe a charged polymer or copolymer that changes the effective charge density on the surface of the stationary phase by a physical stimulus. Thus, JP '551 does not anticipate independent claim 1 and claims that depend therefrom. Applicants respectfully request reconsideration and withdrawal of this rejection.

JP '551 also does not teach or suggest a charged polymer or copolymer that changes the effective charge density on the surface of the stationary phase by a physical stimulus. The materials described in JP '551 are packing materials having modified surfaces. The modified surfaces include reactive groups to which are bonded a temperature-responsive polymer. See Formula 3 of JP '551. There is no teaching or suggestion in JP '551 to include a charged polymer or copolymer in a stationary phase that changes the effective charge density on the surface of the stationary phase. Nothing in JP '551 would provide motivation to a person of ordinary skill to include a charged polymer or copolymer on the surface of the chromatographic packing for any reason. JP '551 is devoid of a teaching or suggestion of charged polymers. Thus, independent claim 1 and claims that depend therefrom are patentable over JP '551. Applicants respectfully request reconsideration and withdrawal of this rejection.

**Independent claim 8 and claims that depend therefrom**

Applicants have discovered a method for separating substances. The method includes retaining substances using a stationary phase including a chromatographic packing chemically modified with a polyalkylacrylamide copolymer having an amino, a carboxyl, or a hydroxyl group and **the hydrophilic/hydrophobic balance on the surface of the stationary phase can be changed by the temperature gradient method** wherein the external temperature is changed stepwise. See independent claim 8. The physical stimulus changes the surface of the effective charge density on the surface of the carrier, making it possible to perform two chromatographic modes, for example, ion-exchange chromatography and reversed phase chromatography, with the stationary phase. See page 6, lines 1-9 of the specification. Substances which have not been able to be separated by conventional methods can be separated by the method of claim 1. See, for example, page 4, lines 16-23 and page 6, lines 17 through page 7, line 6 of the specification.

JP '551 does not describe a stationary phase made of a chromatographic material chemically modified with a polyalkylacrylamide copolymer having an amino, a carboxyl, or a hydroxyl group and the hydrophilic/hydrophobic balance on the surface of the stationary phase can be changed by the temperature gradient method wherein the external temperature is changed stepwise. While JP '551 describes packing material having reactive groups, these reactive groups are needed in order to bond a temperature-responsive polymer to the surface of the chromatographic packing. See paragraph 6 of JP '551. There is no description of packing chemically modified with a polyalkylacrylamide copolymer having an amino, a carboxyl or a hydroxyl group. See Formula 3 of JP '551. Thus, JP '551 does not anticipate independent claim 8 and claims that depend therefrom. Applicants respectfully request reconsideration and withdrawal of this rejection.

JP '551 does not teach or suggest the method of claims 1 or 8. JP '551 does not teach or suggest a packing chemically modified with a polyalkylacrylamide copolymer having an amino, a carboxyl or a hydroxyl group or changing the hydrophilic/hydrophobic balance on the surface of the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise. JP '551 teaches a poly alkyl acrylamide that does not have an amino, carboxyl or hydroxyl group. See Formula 1 of JP '551. There is no teaching or suggestion in JP '551 to include a charged polymer or copolymer in a stationary phase that changes the effective charge density on the surface of the stationary phase. Nothing in JP '551 would provide motivation to a person of ordinary skill to include a polyalkylacrylamide copolymer having an amino, a carboxyl or a hydroxyl group on the surface of chromatographic packing for any reason. JP '551 is devoid of a teaching or suggestion of a polyalkylacrylamide copolymer having an amino, a carboxyl or a hydroxyl group on the surface of chromatographic packing. Thus, independent claim 8 and claims that depend therefrom are patentable over JP '551. Applicants respectfully request reconsideration and withdrawal of this rejection.

## CONCLUSION

Applicants ask that all claims be allowed. Enclosed are a petition for two month extension of time and a check for the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 3-3-03

Harold H. Fox
Reg. No. 41,498

Fish & Richardson P.C.
1425 K Street, N.W.
11th Floor
Washington, DC 20005-3500
Telephone: (202) 783-5070
Facsimile: (202) 783-2331

## Version with markings to show changes made

In the claims:

Claims 12-14 have been cancelled without prejudice.

Claims 5 and 8 have been amended as follows:

--5. (Amended) The separation method as claimed in Claim 3 or 4, wherein said temperature-responsive polymer, with which the surface of the carrier is chemically modified, is a polyalkylacrylamide polymer or copolymer having **an** amino, **a** carboxyl, **or a** hydroxyl **[groups, etc.] group** in the side chains or at the ends.--

--8. (Amended) A method for separating substances characterized by retaining the substances in a stationary phase made of a chromatographic packing chemically modified with a polyalkylacrylamide copolymer having **an** amino, **a** carboxyl, **or a** hydroxyl **[groups, etc.] group**, then changing the hydrophilic/hydrophobic balance on the surface of the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise, and passing the substances through a single mobile phase to thereby separate the same.--